Monoclonal Antibodies, Inc., 802 F.2d 1367, 1379, 231 U.S.P.Q. 81, 90 (Fed. Cir. 1986); *Atlas Powder Co. v. E.I du Pont De Nemours & Co.*, 750 F.2d 1569, 1574, 224 U.S.P.Q. 409, 411 (Fed. Cir. 1984).

The Examiner has stated that Stein et al. discloses an antigen from the Calu3 human lung adenocarcinoma cell line with a molecular weight of greater than 300kDa. The Examiner has further stated that the specification discloses that antibodies which bind the claimed antigen were obtained by using the culture broth of the Calu3 cell line, hence the antigen disclosed by Stein et al. may be the identical antigen of the instant invention, having the same inherent properties such as the binding of particular lectins and monoclonal antibodies. Applicants respectfully disagree.

Applicants submit that Stein et al. used only membrane preparations of Calu-3 as an immunogen. In the abstract of Stein et al., it is stated that "[m]urine monoclonal antibodies (MAbs) reactive with human non-small cell carcinoma of the lung (NSCCL) were produced following immunization with a membrane preparation of Calu-3 . . . ." (Emphasis added). Further, on page 557, first paragraph, of Stein et al., it is stated that "[a] membrane preparation of Calu-3, a human lung adenocarcinoma cell line grown in nude mice, was used as immunogen." Furthermore, page 560, first full paragraph, of Stein et al. states "[a] panel of tissue culture cell lines and normal human blood cells were tested for reactivity with hybridoma supernatant using an indirect immunofluorescence assay which detects binding of the MAb to **cell surface determinants**. As shown in Table 1, the antigen was strongly expressed **on** the immunizing cell line (Calu-3) . . . ." (Emphasis added). This clearly

establishes that the monoclonal antibodies raised in Stein et al. were against components in the membrane of the Calu-3 cells.

To the contrary, the antigen/glycoprotein used to raise antibodies in the present invention is a secreted protein. Page 7, last paragraph, of the specification describes the preparation of the immunogen of the present invention: "An established lung adenocarcinoma cell line, such as Calu-3 (ATCC HTB-55) for example, is cultured in RPMI 1640 medium or MEM medium and then the culture supernatant fluid is recovered. After removing insoluble matter from the thus recovered culture supernatant by centrifugation or using a filter, this is applied to a . . . column to effect adsorption of the antigen in the culture supernatant fluid."

Thus, it is clear that the antigen/glycoprotein of the present invention is a secreted protein found in the supernatant of the cell culture, which is very different from the antigen (i.e., membrane preparation) used by Stein et al. To further support Applicants' argument that the immunogens are different, Applicants direct the Examiner's attention to De Robertis (Cell and Molecular Biology, 7th Ed., pp. 235-7, 1975).

Figure 11-7 of De Robertis depicts secretory and plasma membrane glycoproteins being exocytosed from the cell. However, only the secretory glycoproteins are secreted. The plasma membrane glycoproteins are not secreted, but instead are incorporated into the plasma membrane. In fact, De Robertis states that "[i]n addition to the glycoproteins that are secreted and those that are incorporated into the plasm membrane are others that become incorporated into lysosomes." See page 236, column 1, fourth full paragraph, of De

Robertis et al. Thus, according to the teachings of De Robertis, there are potentially three different types of glycoproteins, those that are secreted, those that are incorporated into the plasma membrane and those that are incorporated into lysosomes.

Therefore, because Stein et al. does not teach each and every element of the claimed invention (i.e., a secreted protein antigen), Stein et al. cannot and indeed does not anticipate the claimed invention.

Accordingly, Applicants respectfully request withdrawal of the rejection of claims 10-11 under 35 U.S.C. § 102(b).

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,

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